REMARKS

The Amendments to the Claims

Applicants have amended claims 4 and 42 to delete, without prejudice, the recitation of the phrase "or a derivative or homolog thereof which *in situ* forms part of the extracellular matrix (ECM) in an animal."

Applicants submit that the amendments constitute no new matter; their entry is respectfully requested.

The Office Action

Applicants thank the Examiner for withdrawing the rejections under 35 U.S.C. § 102(b).

THE REJECTIONS

The Rejections Under 35 U.S.C. § 112 First Paragraph

The Claims Are Enabled And Meet The Written Description Requirement

The Office Action has maintained the rejection of claims 4-5, 12 and 43-44 under 35 U.S.C. § 112, 1st paragraph. The Office Action contends that, since the claimed invention is not supported by either a specific and/or substantial asserted utility or a well-established utility, one skilled in the art would not know how to make and use the claimed invention, for the reasons set forth in the Office Action mailed March 31, 2006. Briefly, the Office Action contends that, while the specification asserts specific utilities for the claimed polypeptides as a molecular marker, the specification does not provide guidance as to how the skilled artisan would measure WARP for extracellular matrix (ECM) integrity. Further, the Office Action contends that the specification does not provide sufficient guidance as to the nature of the changes made to a reference WARP sequence for the skilled artisan to make and use such "derivative" and "homolog" that "in situ form part of the extracellular matrix" commensurate in scope with the claimed invention. In addition, the Office Action has alleged that the phrase "in situ forms part

of the ECM in an animal" as not providing a requisite functional activity for the claimed invention. Applicants respectfully traverse this rejection.

Applicants have amended claim 4, without prejudice, to delete the phrase "or a derivative or homolog thereof which in situ forms part of the extracellular matrix (ECM) in an animal." Applicants respectfully submit that, contrary to the view of the Office Action, the WARP of the instant invention has a clear and credible utility: that of a histological marker. Such utility is disclosed throughout the specification. For example, as disclosed in paragraph [0002] of the specification, which published as US2004-0214349, "the present invention provides a molecular marker of cartilage integrity. The identification of the molecular marker in circulatory or tissue fluid is indicative of disrepair of the extracellular matrix and in particular cartilage such as caused or facilitated by trauma or a degenerative disease or other condition, for example, arthritis or autoimmunity, specifically, a histological marker for cartilage."

Further, as disclosed in paragraph [0022] of the specification, "the identification of WARP permits the detection of mutations in WARP such as those involved in disease conditions such as cartilage disease or arthritis or in a propensity for the development of disease conditions. WARP expression may also be a sensitive indicator of cartilage cell differentiation and is proposed to be useful in monitoring repair, regeneration or other disease processes in a subject. Furthermore, WARP may be used to condition or stabilize stem cells in order to facilitate imprinting of stem cells for tissue replacement therapy."

In support of the asserted utility for WARP as a marker of cartilage integrity, as shown in Figure 3 and Examples 4 and 12, WARP is highly expressed in chondrocytes. In fact, "WARP mRNA levels were 7-fold higher in both primary rib chondrocytes and MCT cells induced to form a hypertrophic chondrocyte-like phenotype, than in MCT cells induced to form an osteoblast-like phenotype and MC3T3 osteoblasts. Expression in chondrocytes was >20-fold higher compared to fibroblasts cell lines and fibroblast-like cells derived from de-differentiated primary chondrocytes. These differences in the level of WARP expression are consistent with those detected by Northern analysis (FIG. 3A) and RT-PCR (FIG. 3B) and indicate that WARP is expressed highest in chondrocytes and at much lower levels in other tissues and cell lines." *See*, paragraph [0149].

Further, as disclosed in paragraph [0150], "expression experiments demonstrate that WARP mRNA is expressed highest in primary rib chondrocytes which contain a mixed population of resting, proliferative, maturing and hypertrophic chondrocytes and in MCT cells induced to express a hypertrophic chondrocyte-like phenotype (Lefebvre et al., 1995, supra). WARP mRNA was undetected or expressed at very low levels in all other tissues and cell lines examined, including MCT cells induced to form osteoblast-like cells. Interestingly, WARP expression was down-regulated when rib chondrocytes were allowed to de-differentiate into fibroblast-like cells suggesting that expression is tightly controlled by the chondrocyte program of gene expression. This is supported by our finding that when MCT cells are induced to change from a hypertrophic-like to an osteoblast-like phenotype by changing the temperature of incubation from 37°C. to 32°C., WARP expression was reduced approximately 6-fold (FIG. 3C)."

In addition, as disclosed in Figure 5 and Example 6, WARP forms higher-order structures in vivo. In particular, Western blot analysis shows that WARP is expressed in newborn mouse cartilage. Further, as disclosed in paragraph [0154], "the results clearly show that WARP is also found in the cartilage matrix in vivo, and the necessity for extraction with a chaotrophic agent suggests that it may be a strongly interacting matrix component."

In view of the above remarks, Applicants submit that the specification provides support for the utility of WARP for identifying these cells using the WARP polypeptide of the instant invention. Moreover, based on the expression profile of WARP, Applicants respectfully submit that any number of specific and substantial utilities for WARP as described in the specification stem directly from its chondrocyte cell and cartilage tissue-specific expression profile. Applicants respectfully submit that the claimed invention is supported by at least a specific and substantial asserted utility such that one ordinarily skilled in the art would appreciate the diagnostic utilities of the WARP polypeptides and know how to use the claimed invention. Accordingly, Applicants respectfully request that the Examiner withdraw the rejections of claims 4-5, 12 and 43-44 under 35 U.S.C. § 112, first paragraph.

The Claims Meet The Written Description Requirement

The Office Action has rejected claims 4-5, 12 and 43-44 under 35 U.S.C. § 112, first paragraph as failing to meet the written description requirement, for the reasons made of record in the Office Action mailed March 31, 2006. The Office Action contends that the specification provides neither a representative number of species (derivative or homolog of WARP) to describe the claimed genus, nor a description of structural features common to a species (derivative or homolog of WARP). Further the Office Action contends that there is no described or art-recognized correlation or relationship between the structure of the invention, the Willebrand domain of the WARP and its function in the ECM. Thus, the OA contends, that one of skill in the art would not envisage, based on the disclosure, the claimed genus or derivative, homolog, 95% or 99% similarity to SEQ ID NO:5, which retain the features essential to the present invention. Applicants traverse in part and amend in part.

As disclosed above, Applicants have amended claims 4 and 43 to delete, without prejudice the recitation of the phrase "or a derivative or homolog thereof which *in situ* forms part of the extracellular matrix (ECM) in an animal." As amended, Applicants submit that the rejection of the terms "derivative" or "homolog" is moot.

With respect to the claimed features of "95% homology" and "99% homology," Applicants respectfully submit that the specification provides support for the terms. The specification in paragraph [0051] defines "homolog" as including "an analogous polypeptide having at least about 65% similar amino acid sequence from another animal species or from a different locus within the same species." Further, as disclosed in paragraph [0144] of the specification, "[t]he human homolog of WARP was identified by searching the genome data with the mouse WARP protein sequence. A match with a predicted protein sequence (hypothetical protein FLJ22215) with very high homology to the mouse WARP was found. ... These sequences are clearly homologs of each other because they share 79% amino acid identity (see FIG. 1C). In addition, if conserved changes are considered in the analysis, they share 95% identity."

Given that Applicants provide written description for "homolog" and a mouse and a human WARP sequence that are 79% identical, or 95% identical of conserved amino acids are considered, Applicants respectfully submit that the presently amended claims satisfy the written

description requirement. Accordingly, Applicant respectfully requests that the Examiner withdraw the rejections of claims 4-5, 12 and 43-44 under 35 U.S.C. § 112, first paragraph.

Conclusion

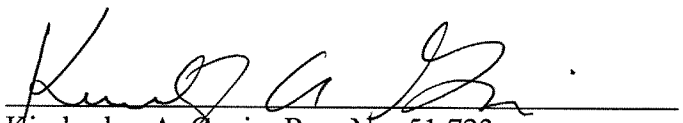
On the basis of the foregoing Remarks, Applicants respectfully submit that the pending claims of the present application are allowable over the prior art of record. Applicants thus respectfully request that the Examiner enter this Response, and withdraw the rejections of the pending claims.

Applicants submit that this Response does not raise new issues for consideration or necessitate the undertaking of any additional search of the art by the Examiner because all of the elements and their relationships were either earlier claimed or inherent in the claims as examined. This Response should therefore allow for immediate action by the Examiner.

Applicant also submits that entry of this Response would place the present application in better form for appeal, should the Examiner dispute the patentability of any of the pending claims. The Examiner is invited to contact the undersigned at (212) 408-2529 if any additional information or assistance is required.

Applicant believes that no additional fee is due. However, Applicant authorizes, in the Fee Transmittal Form the Director to charge payment of any additional fees or credit any overpayment associated with this Response to Deposit Account No. 02-4377.

Respectfully submitted,



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